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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,389	07/01/2005	Yoshifumi Yanagita	12218/67	6379
23838 7590 07/18/2007 KENYON & KENYON LLP 1500 K STREET N.W. SUITE 700 WASHINGTON, DC 20005				
			EXAMINER LILLING, HERBERT J	
			ART UNIT 1657	PAPER NUMBER
			MAIL DATE 07/18/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/541,389

Applicant(s)

YANAGITA ET AL.

Examiner

HERBERT J. LILLING

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 July 2005 and 28 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 July 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>7-1-2005; 7-28-2006</u> . | 6) <input type="checkbox"/> Other: _____  |

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1. Receipt is acknowledged of a preliminary amendment filed July 1, 2005 and two prior art information statements filed July 1, 2005 and July 28, 2006 for this application, which is a 371 national phase application of PCT/JP2004/000416 filed 20 January 2004, claiming priority to Japanese Application No. 2003-011099 filed 20 January 2003. The continuing data should be inserted on page 1 of the specification.

2. Claims 1-20 are now pending in this application.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrison et al ; or Osamu et al . JP 2001/057895 [Reference 1] or Walker et al EP 0046017 or further in view of each other plus further in view of References 2, 3, 4 or 5 for specific claims.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Harrison et al teaches the same process steps Claims 1, 6, 7, 8, 9, 10, 11, 14, 15, 16 and 20 for the claimed subject matter as recited in the Abstract except for the washing of the PHA with water or hydrophilic solvent:

Mechanical cell disruption by high pressure homogenisation or high speed bead mills is currently the general method of choice for the large scale disruption of micro-organisms; however, deleterious effects include the high energy requirement, the need for efficient cooling to prevent the excessive heating of the product and the micronisation of cell debris. Certain chemical treatments for microbial cell disruption alter the permeability of bacteria and yeasts, allowing partial release of soluble products. Such treatments are insufficient for the recovery of granular intracellular products. As cell wall strength has been cited as a major factor influencing the requirements for efficient mechanical disruption, the use of chemical pretreatment to decrease cell wall strength prior to mechanical breakage by homogenisation has been considered. The following treatments were shown to increase the sensitivity of the • Gram-negative bacterium, *Alcaligenes eutrophus*, to disruption: alkaline pH shock, the addition of an anionic detergent, increase of the monovalent cation concentration, the addition of EDTA and enzymic lysis by lysozyme. These pretreatments allow equivalent disruption to be achieved at lower operating pressures or fewer passes through the homogeniser. Alkaline pH pretreatment at pH 10.5 allowed a 37.5% increase in soluble protein release on subsequent homogenisation. An increase of some 30% in soluble protein release was found following prior addition of 0.137 M monovalent cations ( $\text{Na}^+$  or  $\text{K}^+$ ) at 60 °C. Treatment with an anionic detergent showed a considerable decrease in the number of passes required through the homogeniser. Maximum cell rupture can thus be accomplished at reduced energy-inputs.

Abbreviations: HPH- high pressure homogenisation; PHB- poly-3-hydroxybutyrate; SDS- sodium

Harrison et al teaches each of the steps required which includes the physical disruption which is carried out by a high pressures homogenizer for the recovery of PHB

polymer as well as the pretreatment with an enzyme and or an anionic detergent [surfactant].

Osamu et al teaches the same method steps for the recovery of PHA which includes the step of adding an alkali and/or a surfactant to a suspension of microbial cells of PHA-containing microorganism, as noted to be *Alcaligene eutrophus* which contains a transferred PHA synthase gene from *Aeromonas caviae* which reference abstract does not specify that the suspension is aqueous but the Japanese patent indicates that the additives contain water as noted in para [0029]. Osamu teaches in the disclosure on pages 2-3 various copolymers of 3-HB and 3HV.

Osamu clearly indicates the use of a surfactant within the scope of **claim 11**.

The abstract of the Osamu et al reference does not indicate that there is a physical disruption treatment to obtain the PHA from the cell.

Walker et al teaches in Example 1, the process of recovering PBH by adding an alkali to an aqueous suspension of *Alcaligenes eutrophus* which flocculants were separated by decanting from the aqueous suspension.

The reference decanting step is considered to be a physical separation.

#### **Claims 2, 7 and 8-9**

Walker teaches on page 3 that the cells are contacted with a solvent to solubilize the lipids and cells prior to the PHB-extraction.

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Walker also teaches that the addition of alkali is added to increase the pH in the range of 8-12 on page 2, pH 8.5-12 on page 3 and pH 9 in Example 1, which is within the scope of the claimed subject matter.

Walker teaches the use of methanol and acetone for washing as taught in Example 1 for **Claims 12-13**

Masako, Reference 2 or Reference 3, each one teaches the advantages of adding an alkali to an aqueous suspension of PHA containing microorganisms by controlling the temperature and concentration to obtain granular particles of the PHA.

Walker does not indicate any specific alkali.

Masako, Reference 3, teaches in column 3 line 29, LiOH, KOH and NaOH.

**Claims 3-5**

Osamu et al teaches copolymers which includes the 3 HH, 3HB and 3HV.

**Claims 6 and 20**

Harrison et al clearly teaches the same process for employing a high pressure homogenizer as indicated above.

Honma et al, U.S. 6,808,907 teaches commonly used processes for separating the cells from the PHA products as recited:

The method for producing polyhydroxyalkanoate according to claim 13, wherein said step of obtaining the crushed product by crushing cells is performed by at least one selected from the group consisting of ultrasonication method, **homogenizer method, high-pressure crushing method**, bead impact method, milling method, grinding method, and freeze-thawing method.

**Claim 10**

Reference 4 [WO/22659] teaches the addition of an enzyme that aids in the separation and purification of PHA products by dissolving the cell walls, which aids in the recovery of the PHA, which includes the claimed lipid degrading enzymes or/and cell wall degrading enzymes.

**Claims 14-20**

Walker et al teaches the microorganisms as well as Osamu for the PHA containing microorganism.

Thus, the above references are considered to render the instant claims prima facie obvious in view of the teachings of the references either Osamu or/and Walker further in view of the additional references as noted by 2, 3, 4 and 5 absent unexpected or unobvious results or process steps.

Thus, claim 1 which recites the following:

“ A method for recovering a polyhydroxyalkanoate from a polyhydroxyalkanoate-containing microbial cell which comprises the following steps (a) and (b); (a) a step comprising adding an alkali to an aqueous suspension of the polyhydroxyalkanoate-containing microbial cell while stirring and carrying out a physical disruption treatment to disrupt the cell, solubilizing or emulsifying cell substances other than the polyhydroxyalkanoate in said cell, and then separating the polyhydroxyalkanoate from the aqueous suspension, and (b) a step comprising treating the separated polyhydroxyalkanoate with an enzyme

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and/or a surfactant to solubilize impurities adhering to the polyhydroxyalkanoate or to solubilize them after decomposing, and then washing the polyhydroxyalkanoate with a hydrophilic solvent and/or water.”;

Which claimed subject matter is considered to be prima facie obvious in view of the disclosure of the prior art.

Each of the claimed subject matter is clearly anticipated especially in view of step (a) based on Harrison et al, Walker et al or Honma et al for the alkali treating step which includes the physical disruption of the cell.

The step of washing is clearly taught in several of the other references to purify the PHA as taught by Walker et al.

It is acknowledged that not one of the above references anticipates the claimed subject matter for the broad claim 1, however, there is considered absolutely no patentable subject matter that is not obvious over the references of record that demonstrates unexpected or unobvious process steps which includes the alleged unexpected unclaimed process step in the specification which states:

“a treatment at such a low temperature as 20 to 40.degree. C. becomes possible, and the molecular weight decrease might be suppressed to 10% or less even in the case of PHBH. Namely, it is particularly preferred to carry out the physical disruption in a pH level of 9 to 13.5, at 20 to 40.degree. C. When the microbial cells are disrupted under such preferable alkali condition, more reproducible result may be obtained.” ;

which low temperature disruption by a high pressure homogenizer is clearly taught by the prior art as noted above for the same reasons of lower temperature to obtain a greater disruption of the PHA.



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4. **No claim is allowed.**

5. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Lilling whose telephone number is 571-272-0918 and Fax Number is **571-273-8300**, or SPE Jon Weber whose telephone number is 571-272-0925. Examiner can be reached Monday-Friday from about 7:30 A.M. to about 7:00 P.M. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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July 11, 2007



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